

REMARKS

This Amendment responds to the Office Action mailed August 25, 2009. With this Amendment, Applicants amend claims 8 and 11, and cancel claims 9 and 10. Applicants note that the Office has deemed claims 1-7 and 14-22 as being directed to non-elected subject matter and therefore withdrawn these claims from consideration. No new matter has been added with the present Amendment. Support for the Amendment can be found throughout the specification and claims as filed, including, e.g., in original claims 8 and 11, and at pages 11-12 of the specification. Claims 8, 11, 12, and 13 are under consideration with this Amendment.

Objection to the Disclosure

The Office Action objects to the disclosure for not citing the continuation data for the instant application.

In response, and without acquiescing to the propriety of the objection, Applicants submit that the instant Amendment is responsive to the present objection to the disclosure.

Claim Objection

The Office Action objects to claim 8 for recitation of "An isolated DNA a having any of the following nucleotide sequences:".

In response, Applicants submit that the instant Amendment is responsive to the present objection.

Claim Rejections – 35 U.S.C. § 112, First Paragraph

The Action rejects claims 8-13 under 35 U.S.C. 112, first paragraph, as allegedly failing to comply with the written description requirement. In particular, the Action states that “the specification discloses a fluorescent protein from *favia favius* such as SEQ ID NO:1, its specific variants such as SEQ ID NO:12, 14, 16, 18 and 20 having mutations at specific positions, and the nucleotide sequences such as SEQ ID NO:2, 13, 15, 17, 19, and 21 that encoding [sic] the fluorescent proteins” (page 5, first full paragraph). However, the Action alleges that the specification “does not disclose a genus of variants for polynucleotides having a deletion, substitution and/or addition of 1 to 60 nucleotides in the SEQ ID NO:2, 13, 15, 17, 19 or 21 and encoding a fluorescent protein, or polynucleotide fragments of SEQ ID NO:2, 13, 15, 17, 19, or 21.” *Id.* The rejection further alleges that the specification does not provide sufficient guidance as to what structural differences are permissible in the nucleic acid variant that would still produce a functional protein. *Id.*

In response, Applicants submit that the claimed subject matter is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. In particular, Applicants submit that the specification provides the complete sequence structure for a nucleic acid which encodes a novel fluorescent protein from *favia favius* (specification at page 2, lines 7-17 and SEQ ID NOs: 1-2). Applicants further submit that the specification discloses the complete nucleic acid and amino acid sequence structures for five variants thereof, which variants are also fluorescent proteins (SEQ ID NOs: 12-13, 14-15, 16-17, 18-19, and 20-21). Applicants further submit that the variants for which complete sequence data has been provided comprise 1 - 9 amino acid deletions, substitutions, and/or additions. Applicants also submit that

the specification describes mutations which may be made at the following twenty positions with respect to SEQ ID NO: 1: 10, 12, 40, 54, 60, 62, 63, 69, 70, 87, 93, 109, 119, 121, 140, 144, 160, 196, 197, 198.

With regard to the guidance provided by the specification, Applicants submit that Figure 3 shows an alignment of amino acid sequences in proteins encompassed by the claimed subject matter in addition to DsRED and Kaede. Applicants also submit that the specification describes the chromophore shown in an asterisk portion of Figure 3, wherein X may represent any amino acid, Y generally represents tyrosine and optionally an aromatic amino acid such as phenylalanine, tryptophan or histidine, and G represents glycine (see paragraph bridging pages 27-28). Applicants also submit that page 29 of the specification discloses that the shaded portion of Figure 3 highlights residues considered to significantly affect fluorescent properties. Thus, Applicants submit that the specification does provide sufficient guidance as to what structural differences are permissible in the nucleic acid variant that would still produce a functional protein.

To further illustrate the sequence aspects of the claimed subject matter, and in further clarification of the structure/function relationship present in the genus of nucleic acids encompassed by the claims, Applicants further submit herewith Attachments A, B, and C for the Examiner's consideration.

Based at least on the foregoing, Applicants respectfully submit that the specification describes the claimed subject matter in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Accordingly, Applicants respectfully request reconsideration and withdrawal of the rejections under the written description requirement of 35 U.S.C. §112, first paragraph.

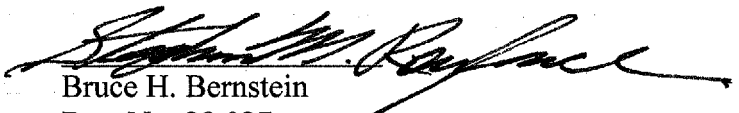
CONCLUSION


In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections of record, and allow all the pending claims.

No additional fee is believed due at this time. If, however, any additional fee is necessary to ensure consideration of the submitted materials, the Patent and Trademark Office is hereby authorized to charge the same to Deposit Account No. 19-0089.

Should there be any questions, the Examiner is invited to contact the undersigned at the below listed telephone number.

Respectfully Submitted,
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| | | 10 | 20 | 30 | 40 | 50 | |
|--------------|-----|------------|------------|------------|------------|------------|-----|
| KKO[Frame 1] | 1 | MSVITSEMKM | ELRMEGAVNG | HKEVITGKGS | GQPFEGIQNM | DLTVIEGGPI | 50 |
| H41pkve#1[Fr | 1 | MSVITSEMKI | ELRMEGAVNG | HKEVITGKGS | GQPFEGIQNV | DLTVIEGGPI | 50 |
| mKikGR1.txt[| 1 | MSVITSEMKI | ELRMEGAVNG | HKEVITGKGS | GQPFEGIQNV | DLTVIEGGPI | 50 |
| mkikgr69.txt | 1 | MSVITSEMKI | ELRMEGAVNG | HKEVITGKGS | GQPFEGIQNV | DLTVIEGGPI | 50 |
| mkikgr10.1[F | 1 | MSVITSEMKI | ELRMEGAVNG | HKEVITGKGS | GQPFEGIQNV | DLTVIEGGPI | 50 |
| mkikgr12.0 D | 1 | MSVITSEMKI | ELRMEGAVNG | HKEVITGKGS | GQPFEGIQNV | DLTVIEGGPI | 50 |
| mkik132.txt[| 1 | MSVITSEMKI | ELRMEGAVNG | HKEVITGKGS | GQPFEGIQNV | DLTVIEGGPI | 50 |
| | | 60 | 70 | 80 | 90 | 100 | |
| KKO[Frame 1] | 51 | PFAPDILTTV | FHYGNRVFVK | YPPEINDYFK | QSFPEGYSWE | RSMSYEDGGI | 100 |
| H41pkve#1[Fr | 51 | PFAPDILTTA | FHYGNRVFVE | YPPEINDYFK | QSFPEGYSWE | RSMSYEDGGI | 100 |
| mKikGR1.txt[| 51 | PFAPDILTTA | FHYGNRVFVE | YPPEINDYFK | QSFPEGYSWE | RSMSYEDGGI | 100 |
| mkikgr69.txt | 51 | PFAPDILTTA | FHYGNRVFVE | YPPEINDYFK | QSFPEGYSWE | RSMSYEDGGI | 100 |
| mkikgr10.1[F | 51 | PFAPDILTTA | FHYGNRVFVE | YPPEINDYFK | QSFPEGYSWE | RSMSYEDGGI | 100 |
| mkikgr12.0 D | 51 | PFAPDILTTA | FHYGNRVFVE | YPPEINDYFK | QSFPEGYSWE | RSMSYEDGGI | 100 |
| mkik132.txt[| 51 | PFAPDILTTA | FHYGNRVFVE | YPPEINDYFK | QSFPEGYSWE | RSMSYEDGGI | 100 |
| | | 110 | 120 | 130 | 140 | 150 | |
| KKO[Frame 1] | 101 | CLATNNITMK | KDGSNCFVNE | IRFDGTVNFA | NGPVMQRKTV | KWEPSTEKMY | 150 |
| H41pkve#1[Fr | 101 | CLATNNITMK | KDGSNCFVNE | IRFDGTVNFA | NGPVMQRKTV | KWEPSTEKMY | 150 |
| mKikGR1.txt[| 101 | CLATNNITMK | KDGSNCFVNE | IRFDGTVNFA | NGPVMQRKTV | KWEPSTEKMY | 150 |
| mkikgr69.txt | 101 | CLATNNITMK | KDGSNCFVNE | IRFDGTVNFA | NGPVMQRKTV | KWEPSTEKMY | 150 |
| mkikgr10.1[F | 101 | CLATNNITMK | KDGSNCFVNE | IRFDGTVNFA | NGPVMQRKTV | KWEPSTEKMY | 150 |
| mkikgr12.0 D | 101 | CLATNNITMK | KDGSNCFVNE | IRFDGTVNFA | NGPVMQRKTV | KWEPSTEKMY | 150 |
| mkik132.txt[| 101 | CLATNNITMK | KDGSNCFVNE | IRFDGTVNFA | NGPVMQRKTV | KWEPSTEKMY | 150 |
| | | 160 | 170 | 180 | 190 | 200 | |
| KKO[Frame 1] | 151 | VRDGVKGDV | NMALLQGGG | HYRCDFRTTY | KAKKVVQLPD | YHYVDHQMEI | 200 |
| H41pkve#1[Fr | 151 | VRDGVKGDV | NMALLQGGG | HYRCDFRTTY | KAKKVVQLPD | YHYVDHQMEI | 200 |
| mKikGR1.txt[| 151 | VRDGVKGDV | NMALLQGGG | HYRCDFRTTY | KAKKVVQLPD | YHYVDHQMEI | 200 |
| mkikgr69.txt | 151 | VRDGVKGDV | NMALLQGGG | HYRCDFRTTY | KAKKVVQLPD | YHYVDHQMEI | 200 |
| mkikgr10.1[F | 151 | VRDGVKGDV | NMALLQGGG | HYRCDFRTTY | KAKKVVQLPD | YHYVDHQMEI | 200 |
| mkikgr12.0 D | 151 | VRDGVKGDV | NMALLQGGG | HYRCDFRTTY | KAKKVVQLPD | YHYVDHQMEI | 200 |
| mkik132.txt[| 151 | VRDGVKGDV | NMALLQGGG | HYRCDFRTTY | KAKKVVQLPD | YHYVDHQMEI | 200 |
| | | 210 | 220 | 230 | 240 | 250 | |
| KKO[Frame 1] | 201 | TSHDKDYNKV | KLYEHAKAHS | GLPRLAK*.. | | | 250 |
| H41pkve#1[Fr | 201 | TSHDKDYNKV | KLYEHAKAHS | GLPRLAK*.. | | | 250 |
| mKikGR1.txt[| 201 | TSHDKDYNKV | KLYEHAKAHS | G*..... | | | 250 |
| mkikgr69.txt | 201 | TSHDKDYNKV | KLYEHAKAHS | S*..... | | | 250 |
| mkikgr10.1[F | 201 | TSHDKDYNKV | KLYEHAKAYS | GTYSKAYEF | EA*..... | | 250 |
| mkikgr12.0 D | 201 | TSHDKDYNKV | KLYEHAKAYS | GTYSKAYEF | EA*..... | | 250 |
| mkik132.txt[| 201 | TSHDKDYNKV | KLYEHAKAYS | GTYSKAYEF | EA*..... | | 250 |

ATTACHMENT A

| | | | | | | | | | | | | | | | | | | | | | | | | | | | | | |
|---------------|-----|----------|--------|--------|--------|--------|-------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|------|-----|-----|-----|
| kikgr.gpt | 1 | MSVITSEM | KIELRM | MEGAVN | GKHKFV | ITGKGS | QPFEG | QNV | DLT | VI | EGG | PLP | FA | ED | IL | TT | AF | HY | GN | RV | FVE | 70 | | | | | | | |
| kikgr1.gpt | 1 | MSVITSEM | KIELRM | MEGAVN | GKHKFV | ITGKGS | QPFEG | QNV | DLT | VI | EGG | PLP | FA | ED | IL | TT | AF | HY | GN | RV | FVE | 70 | | | | | | | |
| kikgr69.gpt | 1 | MSVITSEM | KIELRM | MEGAVN | GKHKFV | ITGKGS | QPFEG | QNV | DLT | VI | EGG | PLP | FA | ED | IL | TT | AF | HY | GN | RV | FVE | 70 | | | | | | | |
| kikgr101.gpt | 1 | MSVITSEM | KIELRM | MEGAVN | GKHKFV | ITGKGS | QPFEG | QNV | DLT | VI | EGG | PLP | FA | ED | IL | TT | AF | HY | GN | RV | FVE | 70 | | | | | | | |
| kikgr110.gpt | 1 | MSVITSEM | KIELRM | MEGAVN | GKHKFV | ITGKGS | QPFEG | QNV | DLT | VI | EGG | PLP | FA | ED | IL | TT | AF | HY | GN | RV | FVE | 70 | | | | | | | |
| mkikgr132.gpt | 1 | MSVITSEM | KIELRM | MEGAVN | GKHKFV | ITGKGS | QPFEG | QNV | DLT | VI | EGG | PLP | FA | ED | IL | TT | AF | HY | GN | RV | FVE | 70 | | | | | | | |
| kikgr.gpt | 71 | YPEE | IVD | YFKQ | SFPEG | YSWERS | MSYED | GGIC | LAT | NNI | TMKK | DG | SNCF | VNEI | RFDG | MN | FP | ANG | PVM | QR | KTV | 140 | | | | | | | |
| kikgr1.gpt | 71 | YPEE | IVD | YFKQ | SFPEG | YSWERS | MSYED | GGIC | LAT | NNI | TMKK | DG | SNCF | VNEI | RFDG | MN | FP | ANG | PVM | QR | KTV | 140 | | | | | | | |
| kikgr69.gpt | 71 | YPEE | IVD | YFKQ | SFPEG | YSWERS | MSYED | GGIC | LAT | NNI | TMKK | DG | SNCF | VNEI | RFDG | MN | FP | ANG | PVM | QR | KTV | 140 | | | | | | | |
| kikgr101.gpt | 71 | YPEE | IVD | YFKQ | SFPEG | YSWERS | MSYED | GGIC | LAT | NNI | TMKK | DG | SNCF | VNEI | RFDG | MN | FP | ANG | PVM | QR | KTV | 140 | | | | | | | |
| kikgr110.gpt | 71 | YPEE | IVD | YFKQ | SFPEG | YSWERS | MSYED | GGIC | LAT | NNI | TMKK | DG | SNCF | VNEI | RFDG | MN | FP | ANG | PVM | QR | KTV | 140 | | | | | | | |
| mkikgr132.gpt | 71 | YPEE | IVD | YFKQ | SFPEG | YSWERS | MSYED | GGIC | LAT | NNI | TMKK | DG | SNCF | VNEI | RFDG | MN | FP | ANG | PVM | QR | KTV | 140 | | | | | | | |
| kikgr.gpt | 141 | KWEP | STE | KMYV | RDG | VLKGD | VEM | ALL | LQ | GG | HY | RCD | FRT | TY | KAK | KV | VQ | LP | DY | HH | VD | HQ | ME | IT | SH | DK | DY | NKV | 210 |
| kikgr1.gpt | 141 | KWEP | STE | KMYV | RDG | VLKGD | VEM | ALL | LQ | GG | HY | RCD | FRT | TY | KAK | KV | VQ | LP | DY | HH | VD | HQ | ME | IT | SH | DK | DY | NKV | 210 |
| kikgr69.gpt | 141 | KWEP | STE | KMYV | RDG | VLKGD | VEM | ALL | LQ | GG | HY | RCD | FRT | TY | KAK | KV | VQ | LP | DY | HH | VD | HQ | ME | IT | SH | DK | DY | NKV | 210 |
| kikgr101.gpt | 141 | KWEP | STE | KMYV | RDG | VLKGD | VEM | ALL | LQ | GG | HY | RCD | FRT | TY | KAK | KV | VQ | LP | DY | HH | VD | HQ | ME | IT | SH | DK | DY | NKV | 210 |
| kikgr110.gpt | 141 | KWEP | STE | KMYV | RDG | VLKGD | VEM | ALL | LQ | GG | HY | RCD | FRT | TY | KAK | KV | VQ | LP | DY | HH | VD | HQ | ME | IT | SH | DK | DY | NKV | 210 |
| mkikgr132.gpt | 141 | KWEP | STE | KMYV | RDG | VLKGD | VEM | ALL | LQ | GG | HY | RCD | FRT | TY | KAK | KV | VQ | LP | DY | HH | VD | HQ | ME | IT | SH | DK | DY | NKV | 210 |
| kikgr.gpt | 211 | KLYE | HAKA | HSGL | PLR | LAK | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | 227 | | |
| kikgr1.gpt | 211 | KLYE | HAKA | HSGL | PLR | LAK | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | 221 | | |
| kikgr69.gpt | 211 | KLYE | HAKA | HSGL | PLR | LAK | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | 221 | | |
| kikgr101.gpt | 211 | KLYE | HAKA | HSGL | PLR | LAK | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | 232 | | |
| kikgr110.gpt | 211 | KLYE | HAKA | HSGL | PLR | LAK | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | 232 | | |
| mkikgr132.gpt | 211 | KLYE | HAKA | HSGL | PLR | LAK | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | ---- | 232 | | |

| clone name | photosensitivity | Green ex | Green em | Red ex1 | Red ex2 | Red em |
|------------|--|-------------|-------------|------------|------------|-----------|
| kikgr | photoconvert to red on irradiation of UV light (360nm) | 507 | 517 | 360 | 583 | 593 |
| kikgr6.9 | photoconvert to red on irradiation of UV light (360nm) | 505 | 516 | 360 | 583 | 593 |
| kikgr10.1 | photoconvert to red on irradiation of UV light (360nm) | 505 | 515 | 359 | 582 | 593 |
| kikgr11.0 | photoconvert to red on irradiation of UV light (360nm) | 505 | 515 | 360 | 582 | 593 |
| kikgr132 | photoconvert to red on irradiation of UV light (361nm) | 505 | 515 | 359 | 580 | 591 |

ATTACHMENT C